(18)

No. 98-1152

IN THE

Supreme Court of the United States

FOOD AND DRUG ADMINISTRATION, *et al.*,
Petitioners,

v.

BROWN & WILLIAMSON TOBACCO CORPORATION, *et al.*,
Respondents.

On Writ of Certiorari to the United States Court of Appeals for the Fourth Circuit

BRIEF OF RESPONDENT BROWN & WILLIAMSON TOBACCO CORPORATION

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WILSON - EPES PRINTING CO., INC. - 789-0096 - WASHINGTON, D.C. 20001

51 pp

QUESTION PRESENTED

The ultimate issue in this case is whether Congress delegated to the Food and Drug Administration ("FDA"), through the Federal Food, Drug, and Cosmetic Act ("FDCA"), the authority to regulate tobacco products as drugs and devices. To sustain its claim to such authority, FDA must establish, *inter alia*, that tobacco products are "articles . . . intended to affect the structure or any function of the body of man" within 21 U.S.C. § 321(g)(1)(C) (drug definition) and 21 U.S.C. § 321(h)(3) (device definition). The specific question addressed in this brief is:

Whether FDA's findings that tobacco products have physical effects on the body when used by consumers in ways that manufacturers foresee and desire, are legally sufficient to establish that these effects are "intended" within the meaning of the FDCA's definitions of "drug" and "device" when:

a) FDA did not find that the manufacturers of tobacco products claim those effects in selling or offering to sell their products;

b) The proper operation of the FDCA requires that manufacturers have the ability to determine, through their claims, the "intended uses" of their products; and

c) For almost a century, as Congress shaped the FDCA, FDA repeatedly and consistently stated to Congress, the courts, and the public, that manufacturer claims are determinative of "intended use," and the courts uniformly implemented FDA's interpretation.

Questions presented by the briefs of other respondents include whether the "effects" found by FDA are cognizable

under the FDCA, even if they are claimed, and whether FDCA authority extends to tobacco products as a class, even though Congress did not provide FDA with tools suitable for regulating tobacco, and instead established a separate comprehensive program to regulate smoking and health which is inconsistent with FDA jurisdiction under the FDCA. Brown & Williamson Tobacco Corporation ("Brown & Williamson") agrees that this case also presents those questions, and it concurs in the presentation thereof by the other respondents.

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STATUTORY PROVISIONS INVOLVED

This brief deals with the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 321 *et seq.*[1] as it has been amended from time to time, and its predecessor, the Pure Food and Drugs Act of 1906, Pub. L. No. 59-384, 34 Stat. 768 (1906) ("Pure Food and Drugs Act").[2]

STATEMENT OF THE CASE

To bring tobacco products within its authority under the FDCA as "drugs" or "devices," FDA must establish that these products are "intended to affect the structure

[1] Reprinted in United States Tobacco Company, *et al.*, Appendix, at 1a-11a.

[2] Reprinted in *id.* at 12a-51a.

or any function of the body of man." 21 U.S.C. §§ 321 (g)(1)(C), 321(h)(3). If tobacco products are not so "intended," they do not meet the FDCA's jurisdictional standard, FDA's assertion of jurisdiction must be set aside, and FDA's tobacco regulations, *see* 61 Fed. Reg. 44,396 (1996), must be declared void.[3]

A. FDA's New Theory Of "Intended Use."

In comments filed in the FDA rulemaking, Brown & Williamson and other manufacturers of tobacco products demonstrated that "intended use" is a term of art under the FDCA, and that it refers to "claims made by the manufacturer in marketing the product."[4] *See* Brown & Williamson Tobacco Corp. *et al.*, "Comments On Regulations Restricting the Sale and Distribution of Cigarettes and Smokeless Tobacco Products," at II-1. (FDA Docket Nos. 95N-0253, 95N-0253J) (1995) ("*Industry Comments*").[5] The *Industry Comments* argued that FDA's new position, under which manufacturer claims no longer are determinative, "would convert every foreseeable off-label use of a drug or device into an intended use attributable to the manufacturer." *Id.* at II-40. As a result, the "FDCA would be unworkable," and the accepted and important use of approved drugs for unlabeled uses—commonly called "off-label uses"—would be undermined. *Id.* at II-40-41.

FDA did not respond to these arguments. It did not discuss how the FDCA would function if unclaimed but

[3] The brief of United States Tobacco Company, *et al.*, demonstrates that FDA also must show that "intended uses" are medical in nature. That is a separate issue from the meaning of "intended."

[4] In some circumstances, the FDCA treats other vendors, *e.g.*, distributors, importers, or retailers, in the same manner that it treats manufacturers. Brown & Williamson uses the term "manufacturer" to mean all relevant vendors.

[5] Copies of Volume II of the *Industry Comments*—discussing the meaning of "intended use"—are lodged with the Clerk of the Court.

foreseeable uses were "intended uses," nor did it explain how its new theory would affect the off-label uses of approved drugs that are central to many fields of medical practice. FDA was clear, however, that its claim to jurisdiction over tobacco products was not based on manufacturer claims, but rather on foreseeable and subjectively desired consumer uses.[6]

FDA made extensive findings concerning the bodily effects of nicotine. *See* 61 Fed. Reg. 44,619, 44,739-44, 44,811-23 (1996). It found that consumers use tobacco products to achieve four allegedly jurisdictional effects: sustenance of addiction, weight loss, sedation, and mental stimulation. *See id.* at 44,665-66, 44,811-23. It further found, from various sources including product design and internal company documents, that manufacturers foresee these unclaimed effects, and subjectively desire that con-

[6] The FDA Brief incorrectly claims that "FDA also relied upon evidence that tobacco manufacturers advertise that tobacco products will provide 'satisfaction,'" and that "'satisfaction' [is] a code word for the pharmacological effects of nicotine." FDA Br. at 7-8 n.2. In fact, FDA's statement justifying the rule explicitly *rejected* a claims-based theory of jurisdiction:

> In concluding that these products [cigarettes and smokeless tobacco] are drug delivery devices within the meaning of the Act, *the Agency is relying not on product labeling or express representations in promotional materials*, but on other relevant objective evidence of intended use.

61 Fed. Reg. 44,619, 45,194 (1996) (footnote omitted) (emphasis added); *see also id.* at 45,198-99. Consistent with this statement, FDA did not identify any brands that currently make "satisfaction" claims. Moreover, a claims-based rationale would apply only to the brands bearing a given claim, and could not justify a categorical rule. Furthermore, FDA did not cite a contemporary study of the meaning of "satisfaction" or other tobacco product claims to consumers. Therefore, contrary to the FDA Brief, FDA's assertion of jurisdiction must, in the first instance, stand based on FDA's theory that the "intended use" of tobacco products is determined by consumer uses that the manufacturer foresees and subjectively desires, and not by manufacturer claims. *See SEC v. Chenery Corp.*, 318 U.S. 80, 94 (1943).

sumers experience them. *See id.* at 44,854-915, 44,986-92. FDA asserted that the four so-called "drug-like" uses are "predominant" or even "nearly exclusive," but it did not quantify those terms. FDA acknowledged that there are "non-drug" uses of tobacco products, but asserted that those uses are "secondary." [7]

To conclude that its findings were legally sufficient to establish that "drug-like" effects are "intended" notwithstanding the absence of manufacturer claims, FDA relied on three propositions, the first two of which explicitly rest on subjective intent. First, FDA said that "persons can be held to 'intend' the reasonably foreseeable consequences of their actions." *Id.* at 44,691. Thus, all foreseeable uses are "intended." *Id.* at 44,692. Second, FDA cited a dictionary to show that "intended" use is what "manufacturers 'have in mind.'" *Id.* at 44,637. It said standardized nicotine levels and internal manufacturer documents show that manufacturers "have in mind" "drug-like" uses. *Id.* at 44,637, 44,642.

[7] FDA's initial jurisdictional analysis accompanying the Proposed Rule said that 75% to 90% of "frequent smokers" are dependent on nicotine. 60 Fed. Reg. 41,453, 41,465 (1995). Obviously, the percentage may be considerably lower for all smokers. In its final Jurisdictional Determination, FDA abandoned the word "frequent" and stated instead that its use of the term "smokers" would reflect the definitions used in the particular study being discussed. 61 Fed. Reg. at 44,730 n.122. Because FDA's final determination that "75% to 90% of smokers" are nicotine dependent rests on multiple studies of differing populations and appears to use the same figure initially attributed only to frequent smokers, what its finding means is unclear. Moreover, FDA found that a group of "young smokers" (those with a median age of 26) had a dependency rate of 51%, and that lower rates are associated with younger age. *Id.* at 44,834. FDA did not discuss the extent, if any, to which tobacco products are used for "drug-like" purposes by non-dependent smokers. FDA agreed that consumers "perceive" themselves to use tobacco for "nonpharmacological" persons such as "taste" or "the ritual" of smoking. *Id.* at 44,823-24. It claimed, however, that these uses are "secondary" to pharmacological effects. *Id.* at 44,824. FDA did not discuss whether the reasons that individuals start smoking are "pharmacological," nor did it explain why it declined to consider such reasons in its analysis of smokers' dependency on nicotine.

Third, FDA stated, "Where consumers use a product predominantly or nearly exclusively to obtain any of the [bodily] effects . . . such evidence . . . alone [is] sufficient to establish manufacturer intent." *Id.* at 44,807. FDA did not derive this proposition of law from the language of the FDCA, nor did it explain how consumer use could establish a manufacturer's objective intent, as opposed to a subjective expectation or desire. Instead, it relied on dictum which suggested that FDA could infer "intended use" from evidence (i) that a product is used "almost exclusively for therapeutic purposes," and (ii) that it "lack[s] . . . a recognized [nondrug] use." *National Nutritional Foods Ass'n v. Mathews*, 557 F.2d 325, 334 (2d Cir. 1977). Finally, FDA asserted that each of the three principles "independently support[ed]" its assertions about "intended use," and that the "cumulative effect" of the principles was conclusive. 61 Fed. Reg. at 45,204.

B. The Lower Courts' Treatment Of FDA's Theory Of "Intended Use."

The district court accepted FDA's theory. *See* Appendix to Petition for Writ of Certiorari, at 102a-120a ("FDA App."). The court of appeals reversed and rejected FDA's "mechanical reading of only the definitions provisions," observing that:

> As noted by the district court, "*no court has ever found that a product is 'intended for use' or 'intended to affect' within the meaning of the [Act] absent manufacturer claims* as to that product's use." Even the FDA does not contend that tobacco manufacturers make any such claims.

FDA App. at 19a (citation omitted).[8] On broader grounds, the court of appeals held that tobacco products

[8] All emphasis herein is added unless otherwise stated.

simply do not "fit into the overall regulatory scheme created by Congress." *Id.* at 20a.

SUMMARY OF ARGUMENT

Since 1906, "intended use" has been a central concept and term of art in federal food and drug regulation. It first was used to refer to what manufacturers communicated through their drug labels, and was later broadened to include manufacturer claims objectively made in "labeling." As Congress shaped the FDCA, FDA repeatedly advised that "intended uses" were determined by manufacturer claims. Courts followed FDA's view, and Congress acted in light of this settled understanding. The critical test was the objective intent expressed in promotional claims; subjective intent was irrelevant.

In crafting the term of art "intended use" over the years, Congress accommodated two objectives: subjecting promotional claims to FDA regulation, including premarket review, and preserving the freedom of medical professionals to practice in accordance with their professional judgment. Congress provided that, if a manufacturer wishes to make a promotional claim to a potential customer, it must first prove to FDA that the claimed use is safe and effective. However, Congress imposed no such duty on a manufacturer for uses the manufacturer does not promote. Nor did Congress empower FDA to regulate unpromoted off-label uses of lawfully sold products. Instead, such uses were left to control by professional medical standards.

FDA's assertion of jurisdiction over tobacco products is inconsistent with the congressionally-enacted meaning of "intended use." FDA now argues that manufacturer claims are not determinative, and that any foreseen, desired, or nearly exclusive use is an "intended use." FDA's new position would prevent the FDCA from working as Congress drafted it, delay the introduction of pioneer drugs, stymie generic competition, interfere with the free-

dom of the medical profession to develop and prescribe beneficial off-label uses, and thus disrupt the harmonious working of the FDCA. FDA's effort to regulate tobacco products by evading the limitations that Congress incorporated into "intended use" is unlawful and must be set aside.

ARGUMENT

I. BEGINNING WITH THE 1906 ACT, MANUFACTURER CLAIMS DETERMINED A PRODUCT'S "INTENDED USE" AND, HENCE, ITS REGULATORY STATUS.

FDA's assertion of jurisdiction over tobacco products rests on its newly-created theory that a manufacturer's subjective intent, not communicated in promotional claims, can establish a product's "intended use." "Intended use" is a term of art that permeates food and drug law.[9] It appears in twenty-seven sections of the FDCA and in over 900 sections of the FDCA's implementing regulations.[10]

The "intended use" concept originated in the Pure Food and Drugs Act of 1906, which focused on manufacturer statements on the product label. Over the decades, that meaning became tightly woven into the fabric of the FDCA. Its lengthy history and its role in the structure and established operation of the FDCA make clear that an "intended use" is one that a manufacturer communi-

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[9] Where Congress relies on a term of art, an agency may not ignore that term of art and supply its own meaning. *See Glaxo Ops. UK Ltd. v. Quigg*, 894 F.2d 392, 397 (Fed. Cir. 1990) (rejecting FDA's interpretation of "active ingredient" where the term was "well-known and well-defined at the time the Act was passed"); *Theiss v. Witt*, 100 F.3d 915, 918 (Fed. Cir. 1996) (en banc) (prohibiting agency from creating its own definition of legislative term of art); *Mississippi Poultry Ass'n v. Madigan*, 9 F.3d 1113, 1114 (1993), *aff'd on reh'g*, 31 F.3d 293 (5th Cir. 1994) (same).

[10] These figures are based on a search of the FDCA and its regulations on West PREMISE 3.7 CD-ROM (updated June 1, 1999) using the query "intend! w/4 use."

cates to potential consumers of its products. A manufacturer's subjective desire or expectation which is not objectively present in promotional claims does not establish an "intended use." To the contrary, as the FDA Brief concedes, the words " 'intended use' (or words to that effect) refer to 'the *objective* intent of the persons legally responsible.' " FDA Br. at 26 (quoting 21 C.F.R. §§ 201.128 (drug), 801.4 (device)). Thus, unclaimed uses—so-called "off-label" uses—are common and important, but they are *not* "intended uses," and they do *not* trigger FDA juirsdiction, even though manufacturers may foresee and subjectively desire them.

A. The Pure Food and Drugs Act of 1906.

The Pure Food and Drugs Act of 1906, Pub. L. No. 59-384, 34 Stat. 768, represented Congress' first enactment of national legislation to protect consumers in their capacity as vulnerable purchasers of medical products. Section 6 of the Act defined "drug" as "all medicines and preparations recognized in the United States Pharmacopoeia or National Formulary for internal or external use, *and any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease of either man or other animals.*" *Id.* at 769. The dual definition encompassed both "medicines and preparations" recognized in one of the designated compendia and "any substance or mixture of substances" that was "intended to be used" to fight "disease."

The Act was "aimed at cheats." H.R. Rep. No. 59-2118, at 7 (1906). As the House Report explained, the Act "simply requires honesty of labeling." *Id.* Thus, the Act targeted manufacturer communications to prospective purchasers, not unstated manufacturer desires. In accordance with its limited purpose, the 1906 Act further limited federal regulatory intervention by making the prohibitions of "adulteration" and "misbranding" turn on deviations between the *labeled* composition of an article and its *actual* composition. *See* §§ 8, 10, 34 Stat. at 770-71. Thus, "intent" as used in the 1906 Act necessarily arose from claims on the label. A broader definition of "intent" would have created the anomaly that a product would have been defined as a drug on a basis that could not be regulated, since only statements on a label could make a product "adulterated" or "misbranded." *See id.* A proper understanding of the limited scope of "intent" in the 1906 Act is important because its concept of "intended use" is the same as the concept of "intended use" codified in the modern FDCA.

In 1911, this Court ruled that the drug labeling provisions of the 1906 Act prohibited false statements about the identity of a drug product, but not false therapeutic claims. *See United States v. Johnson*, 221 U.S. 488, 497 (1911). In 1912, Congress passed the Sherley Amendment, which "prohibited curative or therapeutic effect[s] . . . which [are] false and fraudulent," *see* Pub. L. No. 62-301, 37 Stat. 416 (1912), thus preserving the focus on claims as the basis of regulation.

The 1906 Act employed the language "intended to be used"—not simply "used"—to ensure that only those products labeled as recognized medicines, or labeled with claims that justified viewing the products as medicines, would be regulated. The communicated grounds for sale were controlling, as FDA's predecessor agency confirmed when it addressed tobacco products in 1914:

> Under the Food and Drugs Act, a drug is defined as any substance or mixture of substances, intended to be used for the cure, mitigation, or prevention of disease of either man or other animals. It, therefore, follows that tobacco and its preparations, *when labeled in such a manner as to indicate their use for the cure, mitigation, or prevention of disease, are drugs within the meaning of the act*, and, as such, are subject to the provisions thereof.

> On the other hand, tobacco and its preparations which are not so labeled and are used for smoking or chewing or as snuff and not for medicinal purposes are not subject to the provisions of the act.

U.S. Dep't of Agriculture, Bureau of Chemistry, *Service and Regulatory Announcements*, "No. 13: The Status of Tobacco and its Preparations Under the Food and Drug Act," at 24 (1914) ("*Bulletin*").[11]

B. The Food, Drug, and Cosmetic Act of 1938.

From 1933 to 1938, Congress debated bills that became the FDCA, Pub. L. No. 75-717, 52 Stat. 1040 (1938). The 1938 Act differed from the 1906 Act in critical ways, including the following:

- The concept of "misbranding" was expanded to include claims in the "labeling" as well as on the "label." *See* FDCA, § 502(a), 52 Stat. at 1050 (codified at 21 U.S.C. § 352(a)). "Labeling" includes "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." *Id.* § 201(m), 52 Stat. at 1041 (codified at 21 U.S.C. § 321(m)).[12]
- The definition of "drug" was expanded to include "articles . . . intended to affect the structure or any function of the body," *id.* § 201(g)(3), 52

[11] FDA argues that the words "and are used for smoking or chewing or as snuff and not for medicinal purposes" suggest that consumer use, in addition to claims, would create jurisdiction. However, the better reading of that clause—as confirmed by FDA's long post-1914 practice—is that consumer use is presumed to follow communicated claims.

[12] *Kordel v. United States*, 335 U.S. 345, 348 (1948), held that certain circulars and pamphlets were "labeling" because they were "used in the sale of the drugs." This ruling recognized that the FDCA focused on manufacturer claims communicated in the marketplace.

Stat. at 1041 (codified as amended at 21 U.S.C. § 312(g)(1)(C)), because (1) the prior definition of "drug" related only to treating "diseases," and thus did not encompass certain physiological conditions, such as obesity or shortness, and (2) consumers were vulnerable to fanciful claims of medical cure for such conditions.

- The parallel category of medical "devices," which employed the same "intended use" term of art, *see id.* § 201(h), 52 Stat. at 1041 (codified as amended at 21 U.S.C. § 321(h)), was created because the term "drug" did not apply to all therapeutic products.
- Finally, a requirement of premarket safety review of new drugs was added, *see id.* § 505, 52 Stat. at 1052-53 (codified as amended at 21 U.S.C. § 355).

The statute explicitly limited the scope of FDA premarket safety review to manufacturer claims, and manufacturers were *not* required to demonstrate safety for other uses. A manufacturer had to demonstrate only that its new drug was safe "for use under the conditions prescribed, recommended, or suggested *in the proposed labeling thereof*." 21 U.S.C. § 355(d)(1). The Senate Report on one of the bills that led to the 1938 Act, paralleling the 1914 statement in the *Bulletin*, *supra* p. 10, recognized the continuing tie between manufacturer claims and FDA jurisdiction:

> The use to which a product is to be put will determine the category into which it will fall. . . . *The manufacturer of the article through his representations in connection with its sale can determine the use to which the article is to be put.*

S. Rep. No. 73-493, at 2-3 (1934). Both FDA and the courts have relied widely upon this statement. *See, e.g.,*

56 Fed. Reg. 60,537, 60,546 (1991); *ASH v. Harris,* 655 F.2d 236, 238-39 (D.C. Cir. 1980); *United States v. An Article . . . "Sudden Change,"* 409 F.2d 734, 739 n.3 (2d Cir. 1969).

C. The Drug Amendments of 1962.

In 1962, Congress again expanded the scope of FDA's regulatory oversight. It required a manufacturer of a drug product to make a premarket showing of effectiveness, as well as safety, *for each "use . . . prescribed, recommended, or suggested in the labeling thereof."* Pub. L. No. 87-781, § 102(c), 76 Stat. 780, 781-82 (codified at 21 U.S.C. § 355(d)(1)).[13] Congress made it a violation of the law to market any new drug with an "intended use"—*i.e.*, a use "prescribed, recommended, or suggested in the labeling"—not approved by FDA. *See* 21 U.S.C. §§ 321(p), 331(d), and 355(a). Thus, FDA must now determine that a new drug is safe and effective for *each* "intended use" before permitting it to be marketed. *Id.* § 355(d); *see also id.* § 352(f)(1); FDA Br. at 27 n.5 (all intended uses must be in labeling).

The Senate Committee that drafted the 1962 Amendments considered whether proof that a drug is effective for one "intended use" should permit it also to be promoted for other "intended uses." The Senators discussed the issue of different "intended uses" in terms of "claims":

> A question arose as to the circumstances and extent to which a new claim or change of claim for effectiveness made after the initial approval of a new-drug application could be made without supporting

[13] The effectiveness requirement involved parallel amendments to a number of FDCA provisions: the definition of "new drug," 21 U.S.C. § 321(p)(1); the criteria for new drug applications, *id.* §§ 355(b)(1)(A), 355(d)(5); the criteria that govern FDA's decision to withdraw approval of a new drug application, *id.* § 355(e)(3); and the investigational new drug exemption, *id.* § 355(i).

> evidence to be submitted to the Department under the new-drug procedure. In order to eliminate any possible ambiguity on this point, the term "effectiveness" is incorporated in the committee's substitute amendment. The effect of this change is to require that *all claims for effectiveness,* whether made initially in a new-drug application or at any time thereafter, *must be supported* by "substantial evidence," which term is defined in the substitute amendment.

S. Rep. 87-1744, pt. 2, at 5 (1962).

The outcome described in the Senate Report is codified in 21 U.S.C. § 355(d)(5), which requires a showing of effectiveness for all "conditions of use prescribed, recommended, or suggested in the [drug's] labeling," and in FDA's regulations. *See* 21 C.F.R. § 201.128. If a manufacturer prescribes, recommends, or suggests a new "intended use," it creates a different new drug, *see id.* § 310.3(h)(4), for which a separate approval must be obtained under 21 U.S.C. § 355(a). To obtain such approval, a manufacturer must submit to FDA, pursuant to 21 C.F.R. § 314.70(b)(3), a supplemental new drug application with "substantial evidence" showing that the product is effective and safe for the new "intended use," a use which must be "prescribed, recommended, or suggested in the [drug's] labeling," *i.e.*, claimed.

The 1962 congressional debate made clear that the phrase "use under the conditions prescribed, recommended, or suggested in the labeling" was synonymous with the concept of an "intended use." For example, the bill which became the 1962 Amendments proposed to require a drug to be safe "and effective for use under the conditions prescribed, recommended, or suggested in the proposed labeling." *See* S. 1552, § 4(a)(1) (as introduced). Senator Kefauver, the bill's sponsor, said that his bill would assure "that all prescription drugs are safe and efficacious *for the uses for which they are intended.*" 107 Cong. Rec.

S5640 (daily ed. Apr. 12, 1961) (introducing S. 1552). Similarly, Chairman Harris of the House Commerce Committee described his bill, which included the identical provision requiring drugs to be safe and effective under the conditions claimed in the labeling, as requiring "a showing that new drugs and biologicals are effective *for their intended use*—as well as safe—before they may be marketed." 108 Cong. Rec. H7714 (daily ed. May 3, 1962) (Chairman Harris' remarks on H.R. 11581, Title I, Part A, § 102 (as reported)). *See also id.* at H10839 (daily ed. June 18, 1962) (Statement of Rep. Sullivan).

The Secretary of Health, Education, and Welfare ("HEW"), FDA's parent agency, testified that Chairman Harris' bill—which contained the provision concerning conditions claimed in labeling—would operate "*by requiring that new drugs be shown effective for their intended uses,* as well as safe, before they are marketed." *Drug Industry Act of 1962: Hearings on H.R. 11581 Before the House Comm. on Interstate and Foreign Commerce,* 87th Cong. 61 (1962) (Statement of HEW Secretary Ribicoff) ("*1962 House Hearings*"). Likewise, during hearings on S. 1552, Secretary Ribicoff stated that HEW supported the legislation because "[t]he manufacturer should satisfy FDA that his product is effective *for the purposes claimed* before it is marketed." *Drug Industry Antitrust Act of 1962: Hearings Before the Subcomm. on Antitrust and Monopoly of the Senate Comm. on the Judiciary*, 87th Cong. 2583 (1962) (Statement of HEW Secretary Ribicoff).

The Senate Committee Report said that the bill required "a premarketing showing that all new drugs are effective—as well as safe—*for their intended uses.*" S. Rep. No. 87-1744, pt. 1, at 8 (1962). The House Committee Report stated that, if "the drug is generally recognized by experts to be effective *for the conditions for which it is intended*, it is not a new drug." H.R. Rep.

No. 87-2464, at 8 (1962). Thus, both reports equated "intended uses" with uses claimed in labeling. As the Conference Report acknowledged, "Both the House amendment and the Senate bill required . . . substantial evidence (as defined) of the *effectiveness of the drug for its proposed use.*" H.R. Conf. Rep. No. 87-2526, at 19 (1962). Similarly, FDA's own comments stated:

> The committee has heard testimony about the alleged difficulties of establishing whether a drug will or will not accomplish *its intended purpose.* . . . The drug *companies routinely assert* through promotional material, in labeling and by other means what they believe their products will accomplish. They do not hesitate to make claims. *The only question is whether they should justify these claims or show the facts upon which they are based.*

1962 House Hearings, at 571-72 (Written Comments of George P. Larrick, FDA Commissioner). Thus, both Congress and FDA equated manufacturer assertions with claims and "intended uses."

D. The Medical Device Amendments of 1976.

In 1976, Congress overhauled the FDCA's regulatory regime for medical devices. *See* Pub. L. No. 94-295, 90 Stat. 539 (1976). For "devices intended for human use," Congress established a risk-based classification system, *see* 21 U.S.C. § 360c(a)(1), which requires that certain devices obtain premarket approval for each of their "intended uses." *Id.* §§ 360c(a)(1)(C), 360e(c). As it did in the 1962 Drug Amendments, Congress allowed manufacturers to determine the "intended uses" for which premarket approval would be required.

Congress recognized that the expensive and time-consuming premarket approval requirement could restrict competition by new manufacturers. It authorized FDA to give clearances to "substantially equivalent" follow-on de-

vices as long as they claim *only* the "intended uses" approved for the pre-existing devices they imitate. *See id.* §§ 360c(f)(3), 360c(i)(1)(A). *See also* Food and Drug Administration, Guidance Doc. No. K86-3, *Guidance on the Center for Devices and Radiological Health's Premarket Notification Review Program*, at 7 (1986) ("if a device [seeking a substantial equivalence clearance] has a different "intended use," there is no reason to proceed further to decide whether the devices are substantially equivalent").

Because the 1976 classification system and premarket approval and clearance regime applied only to "devices intended for human use," 21 U.S.C. § 360(k), concern was expressed that a manufacturer who was denied approval might relabel a device for veterinary use but market it for human use. As the FDA's Brief points out, the House Report sought to foreclose such evasion:

> [A] manufacturer of a device that is banned [for human use cannot] escape the ban by labeling the device for veterinary use. The Secretary may consider the ultimate destination of a product in determining whether or not it is for human use, just as he may consider actual use of a product in determining whether or not it is a device.

FDA Br. at 28 (quoting H.R. Rep. No. 94-853, at 14 (1976)) (emphasis added in FDA Brief). The FDA Brief argues that this comment establishes that the FDCA's definitions of "drug" and "device" do not "limit[] the 'intended' effects of a product to those the manufacturer *expressly* claims." *Id.* at 27. However, the House Report does not eliminate the need for claims; it merely confirms that "claims" can be interpreted in context, *e.g.*, ostensible farm animal claims on a product sold in city pharmacies actually may imply a human use. Additionally, because the tobacco reguations do not identify or rely upon any manufacturer claims, either express or implied, and because FDA's assertion of jurisdiction does not rely on such claim interpretation, *see supra* p. 3 and note 6, this point is inapplicable.[14] In fact, FDA comprehensively reviewed the legislative history of the 1976 Amendments in its 1980 administrative determination that it had no jurisdiction over cigarettes. *See* Letter from Mark Novitch for Jere E. Goyan, FDA Commissioner, to John F. Banzhaf, III and Peter N. Georgiades (Nov. 25, 1980). FDA there concluded that the legislative history provided "no evidence" to sustain its jurisdiction. *Id.* at 3.

E. The Drug Price Competition and Patent Term Restoration Act of 1984.

In the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984), Congress authorized an "abbreviated new drug application" ("ANDA") procedure. This procedure permits the manufacturer of a generic version of a previously approved pioneer drug to avoid the expensive and time-consuming testing and review required to obtain approval of a standard "new drug application" ("NDA"). *See* 21 U.S.C. § 355(j). The ANDA process, like the substantial equivalence clearance process for a follow-on medical device, is intended to enhance competition and reduce health-care costs.[15] FDA may not approve an ANDA unless "the labeling proposed for the new drug is *the same* as the labeling approved for the [pioneer] drug." *Id.* §355

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[14] Moreover, because the 1976 Committee Report interprets language enacted 38 years earlier, it is entitled to little weight. *See, e.g., Public Employees Retirement Sys. v. Betts*, 492 U.S. 158, 168 (1989).

[15] The 1984 amendments do *not* change the provisions of the FDCA requiring FDA to approve *each* "intended use" before a drug is commercially distributed. *See, e.g.*, 21 U.S.C. § 355(d). Thus, if a proposed generic drug has an "intended use" that has not been approved for use in the labeling of the pioneer drug, the generic cannot be approved by an ANDA for any use.

(j)(2)(A)(v). *See* H.R. Rep. No. 98-857, pt. 1, at 21 (1984) ("an ANDA may not be approved for a condition of use that has not previously been approved for a [pioneer] drug"). As in the case of devices, however, pioneer drugs commonly have important unapproved ("off-label") uses that are foreseeable to the ANDA applicant and that may be predominant among consumers. Despite the probability that the generic product would be used for off-label uses, Congress permitted the generic manufacturer simply to duplicate the pioneer product's labeling. Thus, Congress again equated "intended uses" with labeled uses, *i.e.*, claimed uses.

F. The Medical Device Amendments of 1997.

In 1997, FDA asked Congress for authority to regulate off-label uses of devices. Congress refused to make such uses "intended uses." *See* Food and Drug Administration Modernization Act, Pub. L. No. 105-115, 111 Stat. 2296 (1997) ("FDAMA"). Instead, it temporarily authorized FDA, in reviewing a submission under 21 U.S.C. § 360(k), to require a manufacturer to include in the proposed labeling of its device a statement of "appropriate information" about an unclaimed use. FDAMA, § 205, 111 Stat. at 2337 (codified at 21 U.S.C. § 360c(i)(1)(E)(i)). *See id.* § 360c(i)(1)(E)(iv) (five-year sunset on FDA authority). Such a statement could be, for example, that there is insufficient information to justify the use. The unclaimed use still is not an "intended use." FDAMA amended the FDCA to include an explicit instruction that "[a]ny determination by [FDA] of the intended use of a device shall be based upon the proposed labeling." *Id.* § 360c(i)(1)(E)(i). *See* S. Rep. No. 105-43, at 27 (1997).[16]

[16] Congress provided that the 1997 legislation would not "affect the question whether [FDA] has any authority to regulate tobacco." FDAMA, § 422, Pub. L. No. 105-115, 111 Stat. 2296, 2380 (1997) (codified at 21 U.S.C. § 321 note). Thus, the temporary authority that FDA was given with respect to some unclaimed uses of devices is not available to FDA here.

II. IN SHAPING THE MODERN FDCA, CONGRESS ACCEPTED FDA'S REPEATED AND CONSISTENT STATEMENTS, CONFIRMED BY THE COURTS, THAT MANUFACTURER CLAIMS WERE DETERMINATIVE OF "INTENDED USE."

Throughout the years that Congress was shaping the modern FDCA—by legislation in 1938, and with major amendments in 1962, 1976, and 1984—FDA consistently and repeatedly advised that manufacturer claims determined "intended use."

A. FDA Repeatedly Advised Congress That Communicated Manufacturer Claims Determine "Intended Use."

Since 1906, FDA has consistently advised Congress and others that only manufacturer statements establish "intended use." Indeed, many of FDA's statements about the meaning of "intended use" referred specifically to tobacco. The Department of Justice accurately summarized FDA's longstanding position in a 1980 brief defending FDA's determination that it lacked jurisdiction to regulate cigarettes:

> In the 73 years since the enactment of the original Food and Drug Act, and in the 41 years since the promulgation of the modern Food, Drug, and Cosmetic Act, the *FDA has repeatedly informed Congress that cigarettes are beyond the scope of the statute absent health claims* establishing a therapeutic intent on behalf of the manufacturer or vendor.
>
> * * * *
>
> [Even before the 1950's, there are many examples] of [FDA's] interpretation that cigarettes and related tobacco products are not a "drug" under the Act *except when there are health claims*, including correspondence between the agency and members of Congress. . . . These records, including correspond-

ence dating from at least as early as 1940, show that the Commissioner's interpretation was in accordance with the contemporaneous construction of the 1938 Act by the persons charged with its administration.

Br. for Appellee, at 14, 22 n.19, *ASH*, 655 F.2d 236. Many examples of the FDA statements described in the *ASH* brief can be cited.

For instance, in 1965 hearings held in response to the 1964 Surgeon General's Report, FDA testified that it "has no jurisdiction under the Food, Drug, and Cosmetic Act over tobacco, *unless it bears drug claims.*" *Cigarette Labeling and Advertising, 1965: Hearings Before the House Comm. on Interstate and Foreign Commerce*, 89th Cong. 193 (1965) (Testimony of FDA Deputy Commissioner Rankin).

Similarly, in 1972 hearings before the Senate Committee on Commerce, the FDA Commissioner submitted a 1963 letter in which FDA's Bureau of Enforcement instructed all FDA Directors of Bureaus, Divisions, and Districts that "[t]he *statutory* basis for the exclusion of tobacco products from FDA's jurisdiction is the fact that tobacco marketed for chewing or smoking *without accompanying therapeutic claims*, does not meet the definitions . . . for food, drug, device or cosmetic." FDA Bureau of Enforcement, May 24, 1963, *reprinted in Public Health Cigarette Amendments of 1971: Hearings Before the Consumer Subcomm. of the Senate Comm. on Commerce*, 92d Cong. 240 (1972). The Commissioner also testified that, "[i]n *Federal Trade Commission v. Liggett and Myers Tobacco Company* (108 F. Supp. 573, 1952), it was held that cigarettes are not drugs within the meaning of the act *unless a therapeutic purpose is claimed.*" *Id.* at 239.[17]

[17] FDA's position was not and is not unique to tobacco. For example, in 1988, the Consumer Product Safety Commission ("CPSC") asked FDA whether home exercise equipment was a medical device. The answer would determine which agency had jurisdiction, since drugs and devices subject to the FDCA are not subject to the Consumer Product Safety Act, 15 U.S.C. § 2052(a)(1)(H). In a letter from FDA to CPSC, FDA recognized that exercise equipment had foreseeable health uses—*e.g.*, "to redevelop muscles or restore motion to joints or for use as an adjunct treatment for obesity"—that would render them medical devices *if claimed*. *See* Letter from FDA Chief Counsel Scarlett to CPSC General Counsel Lacy, at 2 (May 6, 1988) (lodged with the Clerk of the Court). However, FDA said that "home exercise products *for which no medical claims are made* should be regulated as consumer products by CPSC," *id.* (*i.e.*, that they are not FDCA devices).

B. The Courts Consistently Confirmed That Communicated Manufacturer Claims Determine "Intended Use."

FDA's statements that "intended use" depends upon manufacturer claims have strong judicial support. The courts "have always read the . . . statutory definitions employing the term 'intended' to refer to specific marketing representations." *American Health Prods. Co. v. Hayes*, 574 F. Supp. 1498, 1505 (S.D.N.Y. 1983), *aff'd on other grounds*, 744 F.2d 912 (2d Cir. 1984). "The real test is how this product [is] being sold." *United States v. Nutrition Serv., Inc.*, 227 F. Supp. 375, 386 (W.D. Pa. 1964), *aff'd*, 347 F.2d 233 (3d Cir. 1965). As early as *Bradley v. United States*, 264 F. 79 (5th Cir. 1920), courts were holding that "intended use" is based upon claims. In 1953, the Second Circuit held that claims are essential to establish an "intended use." *FTC v. Liggett & Myers Tobacco Co.*, 203 F.2d 955 (2d Cir. 1953) (per curiam), *aff'g* 108 F. Supp. 573 (S.D.N.Y. 1952).[18] *See also An Article . . . "Sudden Change,"* 409 F.2d at 739 n.3 ("[t]he manufacturer of the article, through his representations in connection with the article can determine the use").

[18] The FDCA's definition of "drug" was imported wholesale into the FTC Act provision dividing responsibility between the FTC and FDA. *Compare* 21 U.S.C. § 321(g)(1) *with* 15 U.S.C. § 55(c). Thus, the definition had to have the same meaning in both acts.

In sustaining FDA's position that it lacks jurisdiction over tobacco products as customarily marketed, *ASH* described the "accepted . . . statutory interpretation" as follows:

> the crux of FDA jurisdiction over drugs [lies] in manufacturers' representations as revelatory of their intent. ("The manufacturer of the article, through his representations in connection with its sale, can determine the use to which the article is to be put.") *Such an understanding has now been accepted as a matter of satutory interpretation.*

ASH, 655 F.2d at 238-39 (citation omitted).[19]

In the only two FDA enforcement actions against tobacco products, the manufacturers were making express claims of weight reduction, *see United States v. 354 Bulk Cartons . . . Trim Reducing-Aid Cigarettes*, 178 F. Supp. 847 (D.N.J. 1959), or curing disease, *see United States v. 46 Cartons, More or Less, Containing Fairfax Cigarettes*, 113 F. Supp. 336 (D.N.J. 1953) (including common cold, influenza, pneumonia, scarlet fever, whooping cough, measles, meningitis, tuberculosis, and parrot fever). In each case, FDA's jurisdiction was based on claims. In particular, the *Trim* case showed that, by *claiming* a weight-control use to which (according to FDA) consumers put cigarettes generally, the product became subject to FDA jurisdiction that was not asserted over other brands. *See Trim*, 178 F. Supp. at 851. Claims, not foreseeable use, establish jurisdiction. FDA's claims-based approach in these two cases is consistent with its longstanding interpretation of "intended use" as a claims-based concept.

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[19] Because FDA had shown no inclination to change its statutory interpretation, the court noted that it need not decide whether a change was permissible. *See ASH v. Harris*, 655 F.2d 236, 242 n.10 (D.C. Cir. 1980).

To avoid these precedents, FDA's brief seeks to shore up its argument by relying on dicta in several cases that the "intended use" of a product may "be determined from its label, accompanying labeling, promotional material, advertising and *any other relevant source*." FDA Br. at 28. Each of the cases, however, involved express promotional claims. Further, under the canon of *noscitur a sociis*, "any other relevant source also must relate to claimed uses. *See Gustafson v. Alloyd Co.*, 513 U.S. 561, 575 (1995) (citing the canon of *noscitur a sociis* "to avoid ascribing to one word a meaning so broad that it is inconsistent with its accompanying words, thus giving unintended breadth to the Acts of Congress"). What makes the "other . . . source" relevant is that it is based on manufacturer claims (*e.g.*, statements by sales representatives to potential customers). *See United States v. Articles of Drug for Veterinary Use*, 50 F.3d 497, 500 (8th Cir. 1995).[20]

The case upon which FDA relied in its rulemaking for its new interpretation of "intended use" suggested in dictum that an "intended use" might be established by evidence that high-dose vitamins (i) were used "almost exclusively for therapeutic purposes," when (ii) "*coupled with* lack of a recognized nutritional [*i.e.*, non-drug] use." *National Nutritional Foods Ass'n*, 557 F.2d at 334. FDA cited this dictum, but did not show how it could be derived from the text of the FDCA. In any event, the two premises upon which the dictum is based are not present here. FDA did not find that tobacco products have no

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[20] FDA previously rejected consumer use as an independent basis for "intended use.'" FDA denied a petition that it regulate cigarettes as drugs on the basis of how "cigarettes are used by smokers." FDA said that evidence of consumer use was "no evidence" of the uses intended by manufacturers within the meaning of the FDCA's definitions. *See* Letter from Donald Kennedy, FDA Commissioner, to John F. Banzhaf, III (Dec. 5, 1977). FDA's position was affirmed in *ASH*, *supra* note 19.

recognized non-drug uses; it merely found the non-drug uses to be "secondary." And, although FDA asserts that one of the "drug-like" uses of tobacco—to sustain addiction—is "nearly exclusive," it equates that phrase with the terms "predominant," "widespread," and "common." 61 Fed. Reg. at 44,807, 44,810-11, 45,192. In any event, the very court that originated the "nearly exclusive" concept held that a toxic effect such as addiction is not a basis for finding that a product is a drug or device. *See National Nutritional Foods Ass'n*, 557 F.2d at 334-35.[21]

In sum, as the court of appeals correctly noted, in the 93 years that "intended use" has been central to federal drug law, "*no court has ever found that a product is 'intended for use' or 'intended to affect' within the meaning of the [Act] absent manufacturer claims as to that product's use.*" FDA App. at 19a.

C. The Administrative Examples Offered by FDA Do Not Establish a Different Institutional View of the Importance of Manufacturer Claims.

FDA does not deny that it generally regards manufacturer claims as determinative of "intended use." It asserts, however, that the agency on occasion has regulated products in the absence of claims. The *Industry Comments* lodged with the Court refute FDA's examples in detail. Briefly stated:

- Several of FDA's examples rest on the theory that a word had developed a secondary meaning that made an implied claim (*e.g.*, "hormone," "sunscreen," and "fluoride"). Other examples rest on

[21] FDA's contention that "consumer use can be relevant in determining manufacturer intent," FDA Br. at 28 (*relying on ASH*, *supra* note 19), is, of course, correct in that consumer understanding can help clarify ambiguous claims. But, as *ASH* makes clear, manufacturer claims are determinative, and common usage is relevant only insofar as its helps explain their meaning. *See ASH*, 655 F.2d at 238-40. As noted above, FDA does not here rely on any claims, express or implied.

express claims (*e.g.*, cocaine substitutes and tinted contact lenses).

- One example depends on a listing of thyroid in a medical pharmacopoeia, thereby obviating the need for any "intended use," see 21 U.S.C. § 321(g)(1)(A) (thyroid); another involves the obligation of a drug manufacturer with an investigational approval to avoid uses outside the scope of the approval, *see* 21 C.F.R. § 312.50 (interferon).
- Still others are based on special sources of FDA authority outside the FDCA's drug and device provisions, such as FDA's non-claims-based jurisdiction over radiation emitting products such as sun lamps, *see* 21 U.S.C. §§ 360hh-360ss (no "intended use" standard), and the lenient "appearance-of-violation" standard for import detentions, *see id.* § 381(a).
- Some examples reflect only tentative FDA views (*e.g.*, the proposed fluoride rule) or uncontested actions (*e.g.*, warning letters concerning novelty condoms or khat) that do not represent FDA's institutional position, *see* 21 C.F.R. § 10.85 (advisory opinions).

None of the examples upon which FDA relies was judicially reviewed. However, when a seizure of a cocaine substitute did reach the courts, the court relied on manufacturer claims to establish "intended use." *See United States v. Storage Spaces Designated Nos. "8" and "49"*, 777 F.2d 1363, 1366-67, nn.5, 6 (9th Cir. 1985). Moreover, FDA never brought any of these examples to Congress' attention while it was enacting food and drug legislation over the decades. These miscellaneous examples culled from fifty-seven years of FDCA administration did nothing to shape the meaning of "intended use" in the FDCA, and thus they are not reliable or authoritative guides to the meaning of "intended use" in the FDCA.

D. FDA's "Intended Use'" Regulations Are Consistent With FDA's Longstanding Position That Claims Are Determinative.

The FDA Brief seeks to rely on FDA's 1952 regulations defining the words "intended use (or words to that effect)" for labeling purposes. FDA Br. at 26-27 (citing 21 C.F.R. §§ 201.128, 801.4). FDA is correct that "intended use" has a consistent meaning throughout the FDCA. But the regulations do not support FDA's current interpretation.

FDA's 1952 regulations begin by stating that the controlling standard is "*objective* intent." 21 C.F.R. § 1.106(o) (1952). By contrast, ordinary concepts of intent are subjective. The distinctive concept of "objective intent" reflects that "intended use" is a term of art. Thus, FDA's current reliance on subjective intent is precluded under its own regulations.

The regulations make the special meaning of "intended use" clear by saying that objective intent may be "shown by labeling claims, advertising matter, or oral or written statements"—*i.e.*, claims. It may also be shown by the fact that an article is "offered and used for a purpose" not stated in its labeling or advertising. Mere use for such a purpose is not sufficient; the article must be both offered and used. In context, to "offer[] . . . for a purpose" means more than a physical delivery. It contemplates a claim about the "purpose" for which the offered article is to be used. The claim typically is communicated by oral or written "expressions" but, in the absence of any such "expressions," may be communicated through "the circumstances surrounding the distribution of the article." [22]

[22] Tobacco products typically are sold with express claims, and FDA did not make any finding that the circumstances surrounding the sale of tobacco products communicate any jurisdictional claim to consumers. Moreover, FDA does not rely on any claims, express or implied. *See supra* p. 3 and note 6.

None of FDA's new theories to establish "intended use"—foreseeability, subjective manufacturer knowledge, desire, or intent, internal manufacturer papers, or product design—appears in the regulations.

The final portions of the 1952 regulations address situations in which the manufacturer does not control the distribution chain. If a manufacturer sells to independent distributors and knows they will make drug claims, it is responsible for those claims. But, FDA made no finding, and makes no argument, that such distribution claims occur with tobacco products.[23]

What "objective intent" means is shown by *Articles of Drug*, 50 F.3d 497. The dispute there involved whether a product used to nourish calves also had an "intended use" as a drug. In the warehouse where the product was seized, the government had found brochures that clearly claimed a drug use, *e.g.*, to treat scours. *See id.* at 500. The manufacturer could not plausibly deny that it subjectively foresaw and desired such a use. Indeed, it apparently claimed that drug use in other countries. It explained, however, that it had not yet distributed the brochures in the United States. *See id.* The court acknowledged that the manufacturer's "intended application" of its product could "be derived from any relevant source, including product labels and any promotional materials." *See id.* But it held that "[p]romotional materials are rele-

[23] For purposes of construing the FDCA, FDA's "intended use" regulations are important only as they bear on how Congress understood the concept of "intended use" as it shaped that Act. To our knowledge, FDA never suggested to Congress that the "intended use" regulations were inconsistent with its repeated statements that only claims could establish an "intended use" that would render tobacco products a drug or device, *supra* pp. 19-24, or with the view that important off-label uses do not give rise to "intended uses," *see infra* pp. 28-32. Now that Congress has embodied the "intended use" concept in the FDCA as a term of art, FDA must respect Congress' intent. *See supra* p. 7 and note 9 and *infra* pp. 36-38.

vant to intent [only] so long as they are currently being distributed" or still have a continuing effect after being distributed. *Id.*

In short, only objective intent as shown by claims communicated in the market determines "intended use." Sources such as internal documents that show subjective intent are not "relevant." Nothing in the 1952 regulations supports FDA's assertion of jurisdiction over tobacco products.

III. THE STRUCTURE AND PROPER OPERATION OF THE FDCA PRESUPPOSE THAT "INTENDED USE" IS BASED ON THE CLAIMS MANUFACTURERS COMMUNICATE TO PROSPECTIVE PURCHASERS.

A. Equating Foreseeable Use With "Intended Use" Would Frustrate Congress' Intent to Prevent FDA Interference With the Practice of Medicine.

The FDCA cannot function as Congress intended it if the link between claims and "intended use" is broken. As FDA has explained:

> Congress did not intend FDA to interfere with the practice of medicine. Thus, once a drug is approved for marketing, FDA generally does not regulate how and [illegible] what uses physicians prescribe the drug. A physician may prescribe a drug for uses or in treatment regimens or patient populations that are not listed in FDA-approved labeling.

More Information for Better Patient Care: Hearings on S. 1477 Before the Senate Comm. on Labor and Human Resources, 104th Cong. 82 (1996) (Statement of William B. Schultz, FDA Deputy Commissioner for Policy) ("*Schultz Testimony*"); 59 Fed. Reg. 59,820, 59,821 (1994) (FDA has long recognized that off-label uses are rational and beneficial); FDA, *Use of Unapproved Drugs for Unlabeled Uses*, Drug Bulletin, Apr. 1982, at 4-5 (same); FDA, Compliance Program Guidance Manual, Center for

Devices and Radiological Health Consumer Education Program, FY 92-93, Program No. 7382.900 pt. I, at 7 (1992) ("off-label uses" are "considered within the pratice of medicine").

FDA recognizes that "off label uses of approved products are appropriate, rational, and accepted in medical practice. FDA knows that there are important off label uses of approved drugs." *Shultz Testimony, supra*, at 81. Indeed, the American Medical Association's Vice President for Science and Education has estimated that between forty and sixty percent of all prescriptions are for off-label uses. *See* Fran Kritz, *FDA Seeks to Add Drugs' New Uses to Labels*, Wash. Post, Mar. 29, 1994, Health (Magazine), at 11. "Off-label drug use is common, and even predominant in the treatment of cancer patients." U.S. General Accounting Office, Pub. No. GAO/PEMD-91-14, *Off-Label Drugs: Reimbursement Policies Constrain Physicians in Their Choice of Cancer Therapies*, at 40 (1991). Of the seventeen most commonly used anticancer drugs, five are used off-label at least seventy percent of the time. *See id.* at 22-23. Some off-label cancer uses constitute "state of the art treatment." *Id.* at 11. In the case of AIDS, experts report that between ninety and one hundred percent of pharmaceutical treatments, including the antiretroviral "cocktail" therapies, are off-label. *See* Kenneth P. Berkowitz *et al.*, *Congress Tries To Bridge The 'Label Gap' But Nobody Is Cheering*, Med. Mktg. & Media, Jan. 1998, at 39-40.

Congress had a compelling practical reason for structuring the FDCA to allow off-label uses—medicine simply moves faster than FDA possibly can:

> New uses for drugs are often discovered after FDA approves the package inserts that explain a drug's approved uses. Congress would have created havoc in the practice of medicine had it required physicians to follow the expensive and time-consuming proce-

dure of obtaining FDA approval before putting drugs to new uses.

United States v. Algon Chem. Inc., 879 F.2d 1154, 1163 (3d Cir. 1989) (quoting *Chaney v. Heckler*, 718 F.2d 1174, 1180 (D.C. Cir. 1983), *rev'd on other grounds*, *Heckler v. Chaney*, 470 U.S. 821 (1985)). *See* William L. Christopher, *Off-Label Drug Prescription: Filling the Regulatory Vacuum*, 48 Food & Drug L.J. 247, 261 (1993) (FDA "could not review drugs . . . at a pace equal to that at which physicians discover beneficial off-label uses").[24]

Two examples illustrate the point. First, on July 20, 1999, the *New England Journal of Medicine* posted on its Internet web site an article that would not be printed until a September issue. *See* Bertram Pitt, *The Effect of Spironolactone on Morbidity and Mortality in Patients with Severe Heart Failure*, 341 New Eng. J. Med. 709 (1999) <http://www.nejm.org/content/pitt/lasp>. The article reports that an old drug had proved so effective in preventing heart failure that the study had been interrupted to treat the control group. An accompanying editorial explained that the article was being released via the Internet so that physicians *immediately* could begin off-label use of this "therapeutic potential of an old drug." Karl T. Weber, *Aldosterone and Spironolactone in Heart Failure*, 341 New Eng. J. Med. 753 (1999) <http://www.nejm.org/content/weber/lasp>.

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[24] Because of insurance reimbursement issues, many states have passed statutes endorsing the off-label use of drugs. For example, N.J. Stat. Ann. § 26:1A-36.9(g) provides:

> "Off-label" use of FDA-approved drugs provides efficacious drugs at a lower cost. To require that all appropriate uses of a drug undergo approval by FDA may substantially increase the cost of drugs and delay or even deny patients' ability to obtain medically effective treatment. FDA approval for each use would require substantial expenditure and time to undergo the clinical trials necessary to obtain FDA approval.

Second, "baby aspirin" continues to be marketed even though it is "not usually for kids anymore," due to concern over Reye Syndrome. Rebecca D. Williams, *How to Give Medicine to Children*, FDA Consumer, Jan.-Feb. 1996, at 6, 9.[25] Today, the small pills primarily are taken by adults daily to reduce the risk of heart attack. To avoid making reduction of heart attack an "intended use," however, baby aspirin manufacturers do not claim it. The Bayer Corporation now markets a baby sized (81mg.) tablet as "Aspirin Regimen Bayer," an "Adult Low Strength" product, labeled "for temporary relief of minor aches and pains or as recommended by your doctor." *See* Physicians' Desk Reference for Nonprescription Drugs and Dietary Supplements 607 (20th ed. 1999). On October 23, 1998, FDA approved professional labeling for the physician-supervised daily administration of aspirin to prevent heart attacks *in persons who already have suffered a heart attack*. *See* 63 Fed. Reg. 56,802 (1998). However, that use remains off-label and unapproved for over-the-counter aspirin products. *See id.* at 56,809. Moreover, for those who have not had a heart attack, the daily prophylactic use of baby aspirin is off-label even if given by a doctor's prescription.

Off-label uses of spironolactone and baby aspirin are foreseeable.[26] In the case of baby aspirin, off-label use is "predominant" and most likely "nearly exclusive" for over-the-counter sales. Under FDA's new theory of "intended use," these foreseeable and important uses would be "intended uses," would make spironolactone and baby aspirin misbranded and therefore unlawful, *see* 21 U.S.C. § 331

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[25] FDA Consumer is a magazine published by FDA.

[26] FDA regulations generally require manufacturers that hold new drug approvals to monitor the literature regarding their products. *See* 21 C.F.R. § 314.80(b). Moreover, under product liability principles, drug manufacturers generally are held to the standard of experts on their products. *See Barson v. E.R. Squibb & Sons, Inc.*, 682 P.2d 832, 835-36 (Utah 1984).

(a), because their labels say nothing about these uses, *see id.* § 352(f)(1), and would expose the manufacturers to possible criminal liability, *see id.* § 333(a)(1). If FDA's new theory were to prevail, Congress' goal of avoiding FDA regulation of the practice of medicine would be thwarted.

B. Treating Foreseeable Use as "Intended Use" Would Frustrate the Premarket Approval Processes Enacted by Congress.

Under 21 U.S.C. § 355(d), FDA cannot approve a drug unless *all* of its "intended" uses first are proved safe and effective. The same is true for devices. *See id.* § 360e(d)(2). Under FDA's present theory, no drug or device approval could be granted until *every* foreseeable use was tested and supported. This would wreak havoc on drug and device approvals.

Many drugs and devices originate, or are first approved and used, outside the United States. By the time FDA approval is sought, a range of uses may be documented in the public medical literature. However, some uses are far more difficult to test than others, and some may not appear economically significant enough to justify the considerable expense of separate testing. *See* Michael P. VanHuysen, Note, *Reform of the New Drug Application Process*, 49 Admin. L. Rev. 477, 488-89 (1997). Cost constraints often force manufacturers to target only a few key uses for testing and approval, even though other foreseeable uses may merit supplemental testing and approval.[27] Thus, it may be appropriate for a manufacturer to claim only one or a few uses initially, and to accept the concomitant limits on its labeling claims. Important uses of a new drug or device also may emerge during the often lengthy period of FDA review. *See Algon Chem.*, 879 F.2d at 1163.

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[27] A manufacturer may advertise its product only for its approved, labeled uses. *See* 21 C.F.R. § 202.1(e)(4)(i)(a).

In December 1998, FDA approved LYMErix, a vaccine for a potentially serious tick-borne disease, but approved it only for use in persons *from ages 15 to 70. See* Carol Lewis, *New Vaccine Targets Lyme Disease: New Hope for Diminishing 'Great Masquerader,'* FDA Consumer, May-June 1999, at 12-13. This "intended use" was approved even though "the highest reported rates of Lyme disease are in children 2 to 15 years old." *Id.* at 13. The manufacturer now is studying the vaccine in children. *See* Linell Smith, *Fighting Lyme Disease With a New Vaccination*, Baltimore Sun, June 20, 1999, Home and Family, at 1M. There are no reports or plans to test the drug in persons over seventy, but physicians nonetheless are making it available off-label to those over seventy where they are at risk. *See id.* By permitting the manufacturer of LYMErix to limit its "intended use" to adults, the FDA made the vaccine available more quickly, with over 700,000 doses administered as of June, 1999. *See id.* Under FDA's new view of "intended use," however, the vaccine still would be unavailable because not all foreseeable (and therefore "intended") uses have been approved, or even yet applied for.

C. Expanding "Intended Use" Beyond Claimed Use Would Limit Generic Competition.

The ANDA process to obtain expedited approval of a generic drug, *see* 21 U.S.C. § 355(j), and the substantial equivalence clearance process for follow-on devices, *see id.* §§ 360(k), 360c(f), 360c(i), limit the "intended uses" that may be claimed. The labeling of a generic drug seeking ANDA approval must be substantially identical to that of the pioneer drug. *See id.* §§ 355(j)(2)(A)(v), 355(j)(4)(G); 21 C.F.R. § 314.94(a)(3). A follow-on device must be "substantially equivalent" to the pioneer device, *see* 21 U.S.C. § 360c(f)(1)(A), and have the same "intended use," *see id.* § 360c(i)(1)(A); 21 C.F.R. § 807.92(a)(5). Otherwise, FDA must deny

approval or clearance. *See* 21 U.S.C. §§ 355(j)(4)(G), 360c(i). Thus, a generic or follow-on product is prohibited from having any "intended uses" (*i.e.*, claimed indications) that are not approved for the pioneer product and supported by its labeling.

But circumstances at the time a follow-on application is submitted—generally at the end of the period of patent exclusivity—may be very different from those when the pioneer product entered the market. The medical community's experience with the product often spawns important off-label uses.[28] Indeed, off-label uses now may be predominant, because the original "intended use" may have become largely obsolete, *e.g.*, baby aspirin.

This circumstance presents no problem under the traditional concept of "intended use." As long as the follow-on product does not claim an off-label use in its labeling, the off-label use is not an "intended use," regardless of how foreseeable, common, or desired it may be. Thus, the off-label use does not require separate FDA approval.

By contrast, under FDA's new theory, foreseeable, common, or desired off-label uses automatically are "intended uses," regardless of what the manufacturer claims. A dilemma results. FDA cannot approve a follow-on drug or device until *all* of its "intended uses" are supported by its labeling. *See id.* § 352(f)(1), 21 C.F.R. §§ 201.5, 201.100(c)(1), 801.5, 801.109(c). Yet, FDA cannot approve the follow-on product if its labeled uses differ from those of the pioneer. *See* 21 U.S.C. §§ 355(j)(2)(A)(v), 355(j)(4)(G) (drugs); *id.* §§ 360(k), 360c(i), 21 C.F.R. § 807.92(a)(5) (devices); *see also* 21 U.S.C. § 360c(i)(1)(E)(iv) (substantial equivalence for devices). Of course, the manufacturer of a generic drug or

[28] One such situation is described in *In re Orthopedic Bone Screw Liability Litigation*, 159 F.3d 817 (3d Cir. 1998), *pet. for cert. filed*, 67 U.S.L.W. 3684 (U.S. May 3, 1999) (No. 98-1768).

device could opt to incur the expense and delay of a full new drug application or device premarket approval application, but that approach would defeat the goals of the generic drug approval and substantial equivalence clearance processes. Thus, applied faithfully, FDA's new theory would frustrate the operation of the FDCA's provisions and lead to results contrary to Congress' intent of increasing competition and reducing health care costs.

D. These Problems Cannot Be Cured by FDA's Enforcement Discretion.

To avert these difficulties, FDA might seek to invoke "enforcement discretion" to allow the continued marketing of drugs and devices with unapproved "intended uses," just as it seeks to allow continued sale of tobacco products despite finding them unsafe. Such a regime would be unlawful. *See, e.g.*, *Chaney*, 470 U.S. at 833-34 (agency cannot suspend a statute); *Hoffman-LaRoche, Inc. v. Weinberger*, 425 F. Supp. 890, 894 (D.D.C. 1975) (same).

Even if those difficulties could be surmounted, however, the FDCA has important consequences that are not subject to FDA control. For example, a violation of the FDCA may be a predicate for a state-law tort claim.[29] In addition, challengers to FDA's approvals and clear-

[29] *See, e.g.*, *Talley v. Danek Med., Inc.*, 179 F.3d 154, 160-61 (4th Cir. 1999); *In re Bendectin Litig.*, 857 F.2d 290, 313 (6th Cir. 1988); *Stanton by Brooks v. Astra Pharm. Prods. Inc.*, 718 F.2d 553, 563 (3d Cir. 1983). One example is currently awaiting a decision on petition for a writ of *certiorari*. *See Bone Screw Liab. Litig.*, *supra* note 28. In that case, FDA refused to clear a § 360(k) notification for a product with labeling claiming an established off-label use, but it cleared an amended notification that included only the established labeled uses of the pioneer device. Later, the manufacturer's omission of a foreseen and desired off-label use was held actionable under a state-law tort theory of "fraud on the FDA."

ances could use FDA's new theory of "intended use" to disrupt the current approval process. *See, e.g., Serono Laboratories, Inc. v. Shalala*, 158 F.3d 1313, 1316-17 (D.C. Cir. 1998). Thus, FDA's reliance on agency "discretion" would provide no solution.

IV. BECAUSE FDA'S NEW THEORY OF "INTENDED USE" SUBVERTS THE WILL OF CONGRESS, CONFLICTS WITH THE FDCA, AND RENDERS IT UNWORKABLE, THE REGULATIONS BASED THEREON ARE CONTRARY TO LAW AND VOID.

FDA's claim that statutory analysis begins and ends with the isolated words of the FDCA's drug and device definitions simply is incorrect. In *Commissioner v. Engle*, 464 U.S. 206 (1983), the Commissioner of Internal Revenue similarly had based his statutory interpretation on a single provision of the tax code, without regard to its context or effect on other provisions. This Court rejected the Commissioner's simplistic approach:

> The true meaning of a single section of a statute in a setting as complex as that of the revenue acts, however precise its language, cannot be ascertained if it be considered apart from related sections, or if the mind be isolated from the history of the . . . legislation of which it is an integral part.

Id. at 223. *Engle* holds that the "duty" of courts and agencies is "to find that interpretation which can most fairly be said to be imbedded in the statute, in the sense of being most harmonious with its scheme and with the general purposes that Congress manifested." *Id.* at 217. *See also Gustafson*, 513 U.S. at 569 (the "Act is to be interpreted as a symmetrical and coherent regulatory scheme"); *FTC v. Mandel Bros.*, 359 U.S. 385, 389 (1959) ("our task is to fit, if possible, all parts into a harmonious whole").

An important element of harmony is *consistency*. This Court has resisted theories of statutory construction that require giving inconsistent meanings to the same words in the same statute. *See United States Nat'l Bank of Oregon v. Independent Ins. Agents, Inc.*, 508 U.S. 439, 460 (1993); *BankAmerica Corp. v. United States*, 462 U.S. 122, 129 (1983). It also has avoided attributing new meanings to terms with settled, widely understood, and relied-upon definitions. *See id.* at 130-32. Where, as here, "the business community directly affected *and* the enforcing agencies *and* the Congress have read [a] statute the same way for 60 years," *id.* at 132, interpretive consistency has a powerful claim.

As shown above, the concept of "intended use" has a long history and a settled term-of-art meaning that is deeply imbedded in the FDCA. When that accepted meaning is honored and applied, the Act functions harmoniously as Congress intended. When it is rejected, there is disharmony and inconsistency, and the will of Congress is thwarted. As Brown & Williamson demonstrates, Congress has not only ratified FDA's construction of "intended use,"[30] but, as in *Engle*, Congress has incorporated that meaning into the Act itself.[31]

FDA argues that, under *Chevron U.S.A. Inc. v. NRDC*, 467 U.S. 837 (1984), it may adopt any plausible meaning of a statutory phrase on which it relies. *See* FDA Br. at 19-20. The premise that any *Chevron* deference

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[30] *See Morton v. Ruiz*, 415 U.S. 199, 237 (1974) ("too late now" for agency to change interpretation after it consistently "led Congress to believe" that interpretation); *see also NLRB v. Bell Aerospace Co.*, 416 U.S. 267, 274-75 (1974) ("a court may accord great weight to the longstanding interpretation placed on a statute by an agency charged with its administration"); *United States v. Rutherford*, 442 U.S. 544, 554 n.10 (1979).

[31] *See also* cases cited *supra* note 9.

applies here is erroneous. What FDA attempts here is not mere gap filling or even a routine application of a jurisdictional standard. Rather, it is a quantum regulatory expansion of jurisdiction over an entire industrial sector. The FDA Brief cites no comparable circumstance that was resolved by *Chevron* deference, and we know of none. *Cf. St. Luke's Hosp. v. Secretary of HHS*, 810 F.2d 325, 331 (1st Cir. 1987) (discussing limits of *Chevron*). Moreover, even if FDA's change in position were not entirely "fatal" to its claim of deference, *see Smiley v. Citibank (South Dakota), N.A.*, 517 U.S. 735, 742 (1996), it necessarily weakens any such claim, *see INS v. Cardoza-Fonseca*, 480 U.S. 421, 446 n.30 (1997) ("agency interpretation of a relevant position which conflicts with the agency's earlier interpretation is entitled to considerably less deference than a consistently held agency view").

Finally, a similar deference argument was made in *Engle*, a case decided the same term as *Chevron*, and this Court flatly rejected it. The Court held that the deference "principle [only sets] the framework for judicial analysis; it does not displace it." 464 U.S. at 225. Where, as here, the history and internal logic of a statute show that Congress intended a special meaning, there is simply no room for deference. *See Chevron*, 467 U.S. at 842-43 (both courts and agencies are bound by the clear will of Congress). FDA's attempt to exceed its settled jurisdictional authority by inventing a new meaning for "intended use" is contrary to the understanding of "intended use" imbedded in the definitions of "drug" and "device" and throughout the FDCA.

CONCLUSION

As Congress builds a complex statute such as the FDCA, later provisions come to rest on the foundational concepts already laid down. Early concepts become imbedded in the Act, and are essential to its operation. They are defined and limited by their functions and interconnections. A statute must be read as an organic whole, and the foundational terms must be given a consistent meaning that permits the harmonious functioning of the Act as a whole.

FDA has not approached the FDCA in this fashion. Instead, it has abstracted the definitions of "drug" and "device" from a complex 93-year statutory context. FDA construes the core statutory concept of "intended use" as if it were a fragment scrawled on a wall, and assigns to it a meaning that frustrates congressional intent. The Court should repudiate FDA's opportunism, and require FDA to respect the law Congress has written.

The decision of the Court of Appeals should be affirmed.

Respectfully submitted,

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